

Applicant: Steven P. Adams et al.  
Title: CELL ADHESION INHIBITORS  
Application No.: 10/625,626  
Filing Date: July 24, 2003

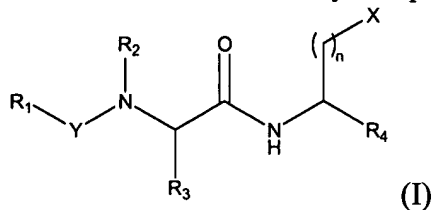
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### Amendments to the claims

This listing of claims will replace all prior versions and listings of the claims.

### Listing of Claims:

1. (Currently amended) A cell adhesion inhibitory compound of formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

X is selected from the group consisting of  $-\text{CO}_2\text{H}$ ,  $-\text{SO}_2\text{R}_5$ , and  $-\text{SO}_3\text{H}$ ;

Y is  $-\text{CO}-$ ,  ~~$-\text{CH}_2-$~~  or  $-\text{SO}_2-$ ;

$\text{R}_1$  is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkyl-substituted alkyl, cycloalkenyl-substituted cycloalkyl, alkoxy, alkenoxy, alkynoxy, alkylamino, alkenylamino, alkynylamino, N-alkylurea-substituted alkyl, alkylcarbonylamino-substituted alkyl, and aminocarbonyl-substituted alkyl;

$\text{R}_2$  is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl;

$\text{R}_3$  is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, hydroxy-substituted alkyl, alkoxy-substituted alkyl, amino-substituted alkyl, thiol-substituted alkyl, alkylsulfonyl-substituted alkyl, (hydroxy-substituted alkylthio)-substituted alkyl, thioalkoxy-substituted alkyl, acylamino-substituted alkyl, alkylsulfonylamino-substituted alkyl, (N-(alkyl, alkenyl or alkynyl) or N,N-(dialkyl, dialkenyl, dialkynyl or (alkyl, alkenyl)-amino)carbonyl-substituted alkyl, carboxyl-substituted alkyl, and amino acid side chains selected from arginine, asparagine, glutamine, S-methyl cysteine, methionine and corresponding sulfoxide and sulfone derivatives thereof, glycine, leucine, isoleucine, allo-isoleucine, tert-leucine, norleucine, alanine, ornithine, glutamine, valine, threonine, serine, aspartic acid, beta-cyanoalanine, and allothreonine;

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R<sub>4</sub> is selected from the group consisting of alkyl, cycloalkyl, alkenyl, cycloalkenyl, and alkynyl;

R<sub>5</sub> is alkyl, alkenyl, cycloalkyl, cycloalkenyl, or alkynyl; and

n is 0, 1 or 2.

2. (Original) The cell adhesion inhibitory compound according to claim 1, wherein R<sub>1</sub> is selected from the group consisting of cyanomethyl, cyclohexylmethyl, methyl, n-hexyl, t-butoxy, t-butylamino, 5-(N'-t-butylurea)pentyl, and 2,2-dimethylpropyl.

3. (Original) The cell adhesion inhibitory compound according to claim 1, wherein R<sub>2</sub> is hydrogen or methyl.

4. (Original) The cell adhesion inhibitory compound according to claim 3, wherein R<sub>2</sub> is hydrogen.

5. (Original) The cell adhesion inhibitory compound according to claim 1, wherein R<sub>3</sub> is selected from the group consisting of 2-(methylsulfonyl)-ethyl, 3-(hydroxy-propylthio)-methyl, 4-(methylsulfonylamino)-butyl, 4-acetylaminoethyl, aminomethyl, butyl, hydroxymethyl, isobutyl, methyl, methylthiomethyl, propyl, N,N-(methylpropargyl)-amino, 2-(methylthio)-ethyl, 2-(N,N-dimethylamino)-ethyl, 4-amino-butyl, t-butoxy-carbonylaminoethyl, sec-butyl, t-butyl, N,N-dimethyl-aminocarbonylmethyl, 1,1-ethano, 1-hydroxyethyl, 1-methoxyethyl, carbonylmethyl, 2-methylsulfinylethyl, and asparagine side-chain.

6. (Original) The cell adhesion inhibitory compound according to claim 5, wherein R<sub>3</sub> is selected from the group consisting of isobutyl, 2-(methylthio)-ethyl, 3-(hydroxypropylthio)-methyl, 2-(methylsulfonyl)-ethyl and 4-acetylamino-butyl, 4-(methylsulfonylamino)-butyl.

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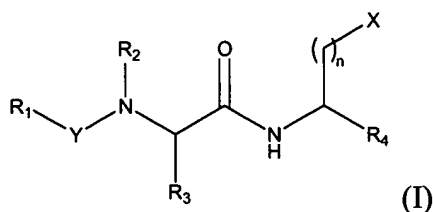
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7. (Original) The cell adhesion inhibitory compound according to claim 1, wherein R<sub>4</sub> is methyl.

8-9. (Cancelled)

10. (Original) The cell adhesion inhibitory compound according to claim 1, wherein n is 1.

11. (Currently amended) A pharmaceutical composition comprising a cell adhesion inhibitory compound of formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

X is selected from the group consisting of -CO<sub>2</sub>H, -SO<sub>2</sub>R<sub>5</sub>, and -SO<sub>3</sub>H;

Y is -CO-, ~~CH<sub>2</sub>~~ or ~~SO<sub>2</sub>~~;

R<sub>1</sub> is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkyl-substituted alkyl, cycloalkenyl-substituted cycloalkyl, alkoxy, alkenoxy, alkynoxy, alkylamino, alkenylamino, alkynylamino, N-alkylurea-substituted alkyl, alkylcarbonylamino-substituted alkyl, and aminocarbonyl-substituted alkyl;

R<sub>2</sub> is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl;

R<sub>3</sub> is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, hydroxy-substituted alkyl, alkoxy-substituted alkyl, amino-substituted alkyl, thiol-substituted alkyl, alkylsulfonyl-substituted alkyl, (hydroxy-substituted alkylthio)-substituted alkyl, thioalkoxy-substituted alkyl, acylamino-substituted alkyl, alkylsulfonylamino-substituted alkyl, (N-(alkyl, alkenyl or alkynyl) or N,N-(dialkyl, dialkenyl,

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dialkynyl or (alkyl, alkenyl)-amino)carbonyl-substituted alkyl, carboxyl-substituted alkyl, and amino acid side chains selected from arginine, asparagine, glutamine, S-methyl cysteine, methionine and corresponding sulfoxide and sulfone derivatives thereof, glycine, leucine, isoleucine, allo-isoleucine, tert-leucine, norleucine, alanine, ornithine, glutamine, valine, threonine, serine, aspartic acid, beta-cyanoalanine, and allothreonine;

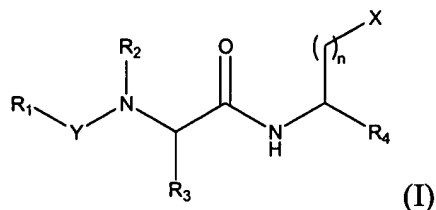
R<sub>4</sub> is selected from the group consisting of alkyl, cycloalkyl, alkenyl, cycloalkenyl, and alkynyl;

R<sub>5</sub> is alkyl, alkenyl, cycloalkyl, cycloalkenyl, or alkynyl; and

n is 0, 1 or 2;

in an amount effective for prevention, inhibition or suppression of cell adhesion;  
and a pharmaceutically acceptable carrier.

12. (Currently amended) A method of preventing, inhibiting or suppressing cell adhesion in a mammal in need thereof comprising the step of administering to said mammal a pharmaceutical composition comprising an effective amount of a cell adhesion inhibitory compound of formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

X is selected from the group consisting of -CO<sub>2</sub>H, -SO<sub>2</sub>R<sub>5</sub>, and -SO<sub>3</sub>H;

Y is -CO-, ~~-CH<sub>2</sub>-~~ or -SO<sub>2</sub>-;

R<sub>1</sub> is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkyl-substituted alkyl, cycloalkenyl-substituted cycloalkyl, alkoxy, alkenoxy, alkynoxy, alkylamino, alkenylamino, alkynylamino, N-alkylurea-substituted alkyl, alkylcarbonylamino-substituted alkyl, and aminocarbonyl-substituted alkyl;

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R<sub>2</sub> is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl;

R<sub>3</sub> is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, hydroxy-substituted alkyl, alkoxy-substituted alkyl, amino-substituted alkyl, thiol-substituted alkyl, alkylsulfonyl-substituted alkyl, (hydroxy-substituted alkylthio)-substituted alkyl, thioalkoxy-substituted alkyl, acylamino-substituted alkyl, alkylsulfonylamino-substituted alkyl, (N-(alkyl, alkenyl or alkynyl) or N,N-(dialkyl, dialkenyl, dialkynyl or (alkyl, alkenyl)-amino)carbonyl-substituted alkyl, carboxyl-substituted alkyl, and amino acid side chains selected from arginine, asparagine, glutamine, S-methyl cysteine, methionine and corresponding sulfoxide and sulfone derivatives thereof, glycine, leucine, isoleucine, allo-isoleucine, tert-leucine, norleucine, alanine, ornithine, glutamine, valine, threonine, serine, aspartic acid, beta-cyanoalanine, and allothreonine;

R<sub>4</sub> is selected from the group consisting of alkyl, cycloalkyl, alkenyl, cycloalkenyl, and alkynyl;

R<sub>5</sub> is alkyl, alkenyl, cycloalkyl, cycloalkenyl, or alkynyl; and

n is 0, 1 or 2;

and a pharmaceutically acceptable carrier.

13. (Original) The method according to claim 12 wherein said method is used for preventing, inhibiting or suppressing cell adhesion-associated inflammation.

14. (Original) The method according to claim 12, wherein said method is used for preventing, inhibiting or suppressing a cell adhesion-associated immune or autoimmune response.

15. (Original) The method according to claim 12, wherein said method is used to treat or prevent a disease selected from the group consisting of asthma, arthritis, psoriasis, transplantation rejection, multiple sclerosis, diabetes and inflammatory bowel disease.